Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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SUPPLEMENTARY APPENDICES

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Cardiothoracic Surgical Trials Network (CTSN)

The members of the Cardiothoracic Surgical Trials Network (CTSN) involved in this study are as follows:

National Heart, Lung and Blood Institute: Marissa A. Miller, Wendy C. Taddei-Peters, Dennis Buxton, Nancy L. Geller, David Gordon, Neal O. Jeffries, Albert Lee**; National Institute of Neurological Disorders and Stroke:** Claudia S. Moy; **Canadian Institutes of Health Research:** Ilana Kogan Gombos, Jennifer Ralph;

Network Chairs: *Toronto General Hospital,* Richard D. Weisel, (Chair); *Christiana Care Health System* Timothy J. Gardner, (Chair Emeritus); *Brigham and Women's Hospital,* Patrick T. O'Gara, (Co-Chair); *Icahn School of Medicine,* Eric A. Rose (Vice-Chair);

Data Coordinating Center: *International Center for Health Outcomes and Innovation Research (InCHOIR), Department of Population Health Science and Policy at the Icahn School of Medicine at Mount Sinai,* Annetine C. Gelijns, Michael K. Parides, Deborah D. Ascheim, Alan J. Moskowitz, Ellen Moquete, Emilia Bagiella, Helena Chang, Melissa Chase, James, Foo, Lopa Gupta, Katherine Kirkwood, Edlira Dobrev, Ron Levitan, Karen O'Sullivan, Jessica Overbey, Milerva Santos, Deborah Williams, Paula Williams, Xia Ye;

Clinical Site Investigators: *Baylor Research Institute :* Michael Mack (PI), Tracine Adame, Natalie Settele, Jenny Adams, William Ryan, Robert L. Smith, Paul Grayburn; *Brigham and Women's Hospital :* Frederick Y. Chen (PI), Anju Nohria, Lawrence Cohn, Prem Shekar, Sary Aranki, Gregory Couper, Michael Davidson, R. Morton Bolman III, Rita Lawrence; *Cleveland Clinic Foundation,* Eugene H. Blackstone (PI), A. Marc Gillinov, Carrie Geither, Leoma Berroteran, Diana Dolney, Kristen Doud, Suzanne Fleming, Roberta Palumbo, Christine Whitman, Kathy Sankovic, Denise Kosty Sweeney; *NHLBI Clinical Research Scholars*: Gregory Pattakos, Pamela A. Clarke; *Columbia University*, Michael Argenziano (PI), Mathew Williams, Lyn Goldsmith, Craig R. Smith, Yoshifumi Naka, Allan Stewart, Allan Schwartz; Daniel Bell, Danielle Van Patten, Sowmyashree Sreekanth; *Duke University*, Peter K. Smith (PI), John H. Alexander, Carmelo A. Milano, Donald D. Glower, Joseph P. Mathew, J. Kevin Harrison, Stacey Welsh; *NHLBI Clinical Research Scholars:* Mark F. Berry, Cyrus J. Parsa, Betty C. Tong, Judson B. Williams; *East Carolina Heart Institute*, T. Bruce Ferguson (PI), Alan P. Kypson, Evelio Rodriguez, Malissa Harris, Brenda Akers, Allison O'Neal; *Emory University*, John D. Puskas (PI), Vinod H. Thourani, Robert Guyton, Jefferson Baer, Kim Baio, Alexis A. Neill; *Hôpital Laval :* Pierre Voisine (PI), Mario Senechal, François Dagenais, Kim O'Connor, Gladys Dussault, Tatiana Ballivian, Suzanne Keilani; *Inova Heart & Vascular Institute :* Alan M. Speir (PI), Patrick Magee, Niv Ad, Sally Keyte, Minh Dang; *Jewish Hospital :* Mark Slaughter (PI), Marsha Headlee, Heather Moody, Naresh Solankhi, Emma Birks; *Mission Hospital :* Mark A. Groh (PI), Leslie E. Shell, Stephanie A. Shepard, Benjamin H. Trichon, Tracy Nanney, Lynne C. Hampton, Ralph Mangusan; *Montefiore-Einstein Heart Center, New York, NY,* Robert E. Michler (PI), David A. D'Alessandro, Joseph J. DeRose, Jr., Daniel J. Goldstein, Ricardo Bello, William Jakobleff, Mario Garcia, Cynthia Taub, Daniel Spevak, Roger Swayze, Nadia Sookraj; *Montreal Heart Institute*, Louis P. Perrault (PI), Arsène-Joseph Basmadjian, Denis Bouchard, Michel Carrier, Raymond Cartier, Michel Pellerin, Jean François Tanguay, Ismael El-Hamamsy, André Denault, Jonathan Lacharité, Sophie Robichaud; *NIH Heart Center at*

Suburban Hospital, Keith A. Horvath (PI), Philip C. Corcoran, Michael P. Siegenthaler, Mandy Murphy, Margaret Iraola, Ann Greenberg; *Ohio State University Medical Center:* Chittoor Sai-Sudhakar (PI), Ayseha Hasan, Asia McDavid, Bradley Kinn; *Sacre-Cœur de Montreal :* Pierre Pagé (PI), Carole Sirois; *University of Maryland :* James S. Gammie (PI), Cindi A. Young, Dana Beach, Robert Villanueva; *University of Pennsylvania,* Michael A. Acker (PI), Y. Joseph Woo, Mary Lou Mayer; *University of Southern California :* Michael Bowdish (PI), Vaughn A. Starnes, David Shavalle, Ray Matthews, Shadi Javadifar, Linda Romar; *University of Virginia,* Irving L. Kron (PI), Gorav Ailawadi, Karen Johnston, John M. Dent, John Kern, Jessica Keim, Sandra Burks, Kim Gahring;

Protocol Review Committee: David A. Bull (Chair); Patrice Desvigne-Nickens, Executive Secretary; Dennis O. Dixon, Mark Haigney, Richard Holubkov, Alice Jacobs, Frank Miller, John M. Murkin, John Spertus, Andrew S. Wechsler;

Data and Safety Monitoring Board: Frank Sellke (Chair); Cheryl L. McDonald, Executive Secretary; Robert Byington, Neal Dickert, Dennis O. Dixon, John S. Ikonomidis, David O. Williams, Clyde W. Yancy;

Medical Monitors: James C. Fang, Nadia Giannetti, Wayne Richenbacher;

Overall Event Adjudication Committee: Vivek Rao (Chair); Karen L. Furie, Rachel Miller, Sean Pinney, William C. Roberts, Mary N. Walsh;

Echocardiography Core Lab: Judy Hung (PI), Xin Zeng, Niamh Kilcullen, David Hung; **Cardiopulmonary Testing Core Lab:** Steve Keteyian (PI), Heather Aldred, Clinton Brawner; **Neurocognitive Core Lab:** Joseph Mathew (PI), Jeffrey Browndyke, Yanne Toulgoat-Dubois

Assessing Degree of Mitral Regurgitation

Severe MR was defined by an effective regurgitant orifice area (EROA) $\geq$ 0.4 cm^2. If the EROA was less than 0.4 cm^2, the assessment of MR severity was guided by jet area/left atrial area ratio, vena contracta, density of the mitral systolic continuous wave Doppler profile, pulmonary vein systolic flow pattern, and left-sided chamber dimensions. TTE will be performed using parasternal, apical, and subcostal views according to a standardized echo study protocol.

1. Quantification of MR

Quantification of mitral regurgitation was performed according to the recommendations of the American Society of Echocardiography Recommendations for evaluation of the severity of native valvular regurgitation[1]. This approach integrates multiple Doppler and 2D imaging criteria to grade MR categorically as mild; moderate; or severe. The primary quantitative measure of mitral regurgitation was effective regurgitant orifice area (EROA)[2-4].

The primary method used to calculate EROA was:

a. PISA (Proximal Isovelocity Surface Area) method.

$$EROA = \frac{6.28 \; x \; radius^2{}_x \; aliasing \; velocity}{Peak \; MR \; velocity}$$

Using this technique, flow convergence area proximal to mitral regurgitant orifice visualized on echocardiography was used to calculate the rate of mitral regurgitant flow and effective regurgitant orifice area (EROA). Regurgitant flow converges to the regurgitant orifice with multiple isovelocity hemispheric configurations. Manipulation of the color flow map identifies a proximal isovelocity surface area (PISA) at a certain aliasing velocity, which is equal to the velocity of the PISA. The region of interest centered on the regurgitant orifice and PISA needs to be zoomed with color-flow imaging and the zero baseline of the color flow map is shifted downward to increase the radius of the PISA. It is recommended that the aliasing velocity be set at 25-40 cm/s. PISA is calculated as 2 л x $radius^2$. Therefore, flow rate at the PISA is calculated as 6.28 x $radius^2$ x aliasing velocities. It is divided by peak MR velocity to obtain the EROA. Peak MR velocity is obtained by continuous-wave Doppler from the apex. Mitral regurgitant volume (RVol) was calculated by multiplying MR TVI by EROA.

The Quantitative Flow method was used as an alternate method to calculate EROA if the PISA method is not measurable. Flow rate and stroke volume can also be estimated using a combination of PW Doppler and two-dimensional measurements. The hydraulic orifice formula states that the volume of blood crossing any valve-annulus is the product of the cross-sectional area (CSA) and the velocity time integral (VTI) of flow at the annulus. In the presence of mitral regurgitation, the diastolic flow across the mitral annulus represents both the systolic forward stroke volume and systolic regurgitant volume. Subtracting the forward stroke volume (across a nonregurgitant aortic or pulmonic valve) from this diastolic volume, yields the mitral RVol. The EROA was subsequently derived by dividing the RVol by the MR VTI.

The EROA was used as the measure of MR severity, because (1) it is objective, and (2) because it is less load dependent than regurgitant volume. MR shall be graded by the following scale:

- <20 mm^2 = mild MR
- 20-40 mm^2 = moderate MR
- >40 mm^2 = severe MR

In using MR for statistical calculations, the PISA value will be treated as a continuous variable. PISA has significant limitations (e.g. non-spherical or multiple jets), but will not be 'overcalled' for the purpose of this study.

In addition to the EROA quantitative measure, the integrated method applies all aspects of the color Doppler jet including jet area/Left atrial area ratio and vena contracta. In addition, supportive data such as left atrial size, E wave peak, and presence of pulmonary vein flow reversal will be incorporated into the assessment.

1. COLOR DOPPLER CRITERIA

	Mild	**Moderate**	**Severe**
Color Flow Jet Area	< 20% of LA area)	20% to 39% of LA area	Large central jet (usually > 10 cm2 or > 40% of LA area) or variable size wall- Impinging jet swirling in LA
VC width (cm)	< 0.3	0.3 – 0.69	≥ 0.7

2. SUPPORTIVE CRITERIA

	Mild	**Moderate**	**Severe**
Structural Doppler Parameters			
LA size	Normal	Normal or dilated	Usually dilated
LV size	Normal	Normal or dilated	Usually dilated
Mitral leaflets or support apparatus	Normal or abnormal	Normal or abnormal	Abnormal/ Flail leaflet/ Ruptured papillary muscle
Mitral inflow - PW	A wave dominant	Variable	E wave dominant (E usually 1.2 m/s)
Jet density - CW	Incomplete or faint	Dense	Dense
Jet contour – CW	Parabolic	Usually parabolic	Early peaking-triangular
Pulmonary vein flow	Systolic dominance[§]	Systolic blunting[§]	Systolic flow reversal[†]

For MV repair group, the same method (integrative technique) for grading MR for baseline echocardiograms was applied, because ring annuloplasty has less acoustic shadowing and color

Doppler components of the mitral regurgitant jet (PISA region, vena contracta and distal jet) can be visualized.

Grading MR in setting of a mitral valve prosthesis was performed using criteria based on the American Society of Echocardiography Guidelines Criteria (Zoghbi WA, Chambers JB, Dumesnil JG, et al. Recommendations for evaluation of prosthetic valves with echocardiography and doppler ultrasound: a report From the American Society of Echocardiography's Guidelines and Standards Committee and the Task Force on Prosthetic Valves, developed in conjunction with the American College of Cardiology Cardiovascular Imaging Committee, Cardiac Imaging Committee of the American Heart Association, the European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography and the Canadian Society of Echocardiography, endorsed by the American College of Cardiology Foundation, American Heart Association, European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography, and Canadian Society of Echocardiography. J Am Soc Echocardiogr 2009; 22:975.

Multiple Imputation of Missing LVESVI Values

The choice of the Wilcoxon Rank-Sum test for the primary analysis was motivated by the expectation of a relatively substantial amount of non-ignorable missing data, primarily due to patient death. These missing data cannot be considered ignorable, and we were hesitant to impute such data using models whose assumptions would not be testable. Absent these concerns, the primary analysis would be by analysis of covariance.

The Wilcoxon Rank-Sum test allows a straightforward incorporation of patients with non-ignorable missing data into the analysis; thereby, avoiding the potential bias of relying on a complete case analysis or on an analysis that assumes the missing data mechanism is missing at random (MAR). For the analysis, patients who die were assigned ranks lower than the lowest observed rank, in ascending order based on the time of death (earliest to latest). Patients whose missing data were determined by independent adjudicators to be due to severity of illness were given the next lowest set of tied ranks. Patients with missing data not due to severity of illness or mortality will have their LVESVI imputed via multiple imputation (Rubin) assuming that the data are MAR, i.e., the missing nature of the variable is independent of the value of the variable given the observed data.

The specific imputation model used included age, sex, and LVESVI measurements obtained at times earlier than 24 months. The main feature of the imputation approach was the creation of a set of clinically reasonable imputations for change in LVESVI for each patient with missing data. This was accomplished using a set of 15 repeated imputations created by the predictive model based on the majority of participants with complete data. The imputation model reflects uncertainty in the modeling process and inherent variability in patient outcomes, as reflected in the complete data. After the imputations were completed, all of the data (complete and imputed) were combined and the analysis performed for each imputed-and-completed dataset. Rubin's method of multiple (i.e., repeated) imputation was used to combine the results of the 15 imputations into a single statistic for testing the between group difference.

A total of 23 patients (9.2%) had LVESVI imputed at 12 months and 42 patients (16.7%) had LVESVI imputed at 24 months.

Figure S1 Consort Diagram

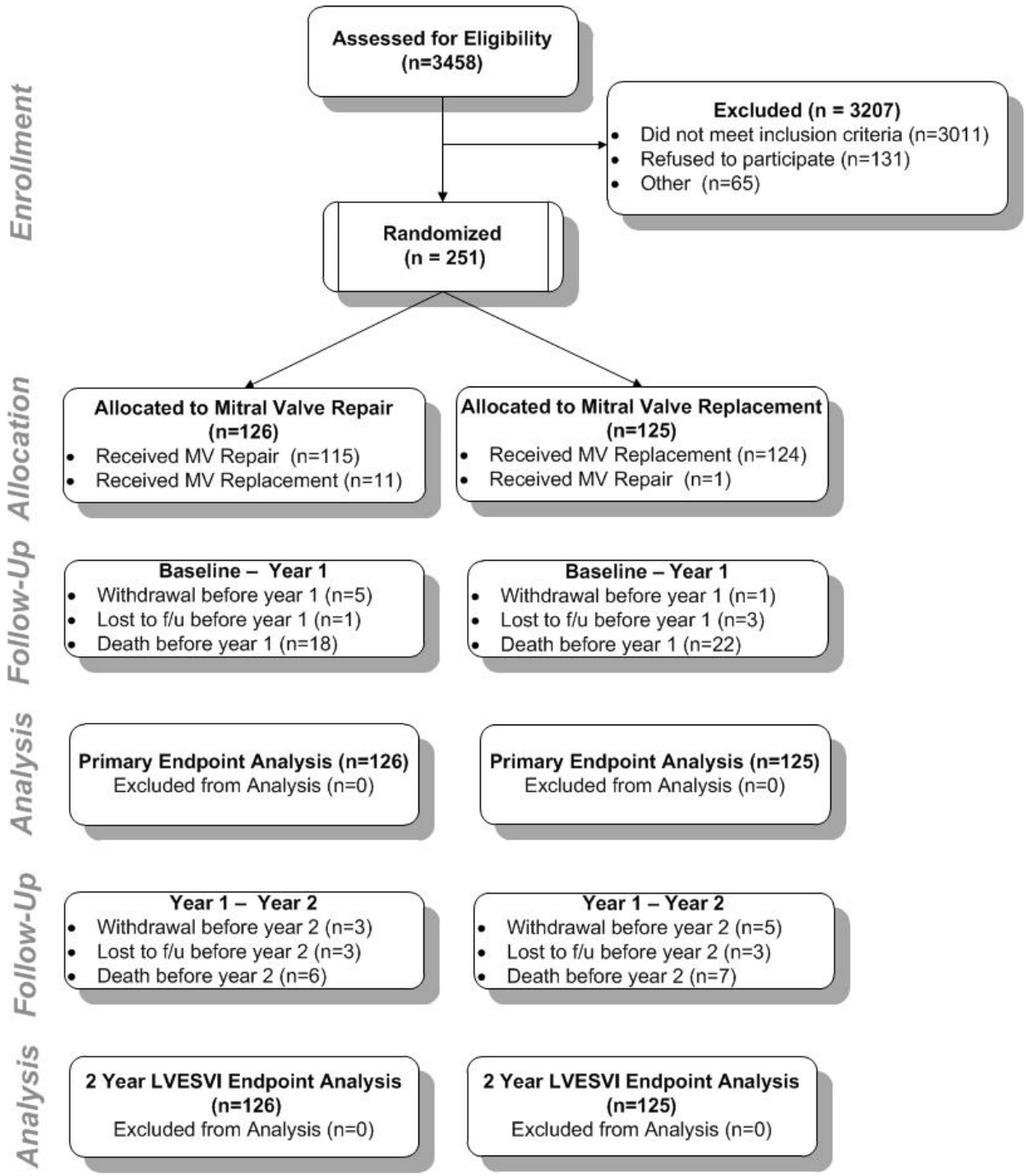

Table S1. Baseline and Operative Characteristics of the Patients*

Characteristic	Repair (N=126)	Replacement (N=125)
Male	77 (61.1)	78 (62.4)
Age (yr)	68.9 ± 10.2	67.9± 9.0
White	104 (82.5)	98 (78.4)
Hispanic	13 (10.3)	11 (8.8)
Diabetes	48 (38.1)	41 (33.1)
Renal Insufficiency	29 (23.0)	40 (32.0)
Prior CABG	24 (19.0)	23 (18.4)
Prior PCI	50 (39.7)	40 (32.0)
Heart Failure	89 (70.6)	91 (72.8)
Myocardial Infarction	99 (78.6)	88 (70.4)
Atrial Fibrillation	45 (35.7)	35 (28.0)
ICD	23 (18.3)	17 (13.6)
Stroke	14 (11.1)	11 (8.8)
LVESVI (mL/m^2)	61.1 ±26.2	65.7±27.3
LVEF (%)	42.4 ± 11.5	40.0 ± 11.4
EROA (cm^2)	0.40 ± 0.17	0.39 ± 0.11
Angina Scale (CCSC)‡ – None	57 (45.2)	70 (56.0)
Angina Scale (CCSC)‡ – Class III & IV	31 (24.6)	21 (16.8)
NYHA‡ – Class III & IV	73 (57.9)	78 (62.4)
MLHF‡	46.1 ± 27.2	50.0 ± 27.4
SF-12 Physical Health Score	37.3 ± 8.1	37.2 ± 7.2
SF-12Mental Health Score	47.9 ± 7.7	47.8 ± 9.1
EuroQOL	53.0 ± 24.6	53.8 ± 23.3
Concomitant procedure – CABG	93 (73.8)	94 (75.2)
Concomitant procedure – Tricuspid Valve Repair	16 (12.7)	22 (17.6)
Concomitant procedure – Atrial Maze	15 (11.9)	16 (12.8)
Duration of aortic cross-clamping (min)	98.9 ± 44.2	106.7 ± 41.6
Duration of cardiopulmonary bypass (min)	138.6 ± 53.4	151.0 ± 49.8

*Plus-minus values are means ± SD, categorical values are n (%)
‡CSCC = Canadian Cardiovascular Society Classification; NYHA = New York Heart Association Functional Class: 1(best) – 4 (worst); MLHF= Minnesota Living with Heart Failure questionnaire: 0 (best) – 105 (worst)